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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/050,231	01/16/2002	William H. Hildebrand	6680.036	8620

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EXAMINER	
VANDERVEGT, FRANCOIS P	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/050,231	HILDEBRAND ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 31-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 31-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12282004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation-in-part of U.S. Application Serial Number 10/022,066, which claims the benefit of the filing date of provisional application 60/261,978.

Claims 1-31 were originally pending and subject to restriction.

Claims 18-30 were previously canceled.

Claim 17 has been newly canceled.

New claims 32-42 have been added.

Claims 1-16 and 31-42 are currently pending and are the subject of examination in the present Office Action.

Election/Restrictions

1. Claims 1-16 and 31-42 are not being examined as they pertain to the non-elected species of MHC class II molecules as part of the complex. Applicant is reminded that the claims would not be meaningful as pertaining to MHC class II because MHC class II complexes do not comprise beta-2-microglobulin as recited in the base claims.

2. **In view of Applicant's amendment filed December 28, 2004, the following grounds of rejection are maintained.**

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-9, 12-16, 31-33, 35, 36 and 39-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Celia et al. (Proc. Nat. Acad. Sci. (USA) [1999] 96:5634-5639; AT on form PTO-1449, of record).

It was previously stated: "Celia teaches complexes comprising recombinant soluble MHC class I molecule-peptide complexes captured on the surface of liposomes in an orientation that allows them to bind to a T cell receptor on a T cell (Abstract in particular). Celia teaches that the MHC-peptide complexes are tagged with a histidine tail that allows the complex to bind chemically modified lipids, anchoring the complex to the liposome (Abstract, paragraph bridging pages5635-5636 and Scheme 1 in

particular). Celia further teaches that, because the MHC:peptide complexes are properly oriented, the artisan would expect that the liposome complexes would be capable of stimulating T cells. Claims 4-7 and 12-17 are included in this ground of rejection because the product is perceived to be the same, irrespective of the manner in which it is made. The prior art teaching anticipates the claimed invention."

Applicant's arguments filed December 28, 2004 have been fully considered but they are not persuasive.

Applicant has amended the claims to recite that the beta-2-microglubulin of the complex is native to and endogenously expressed in a host cell and that the peptide bound to the antigen binding groove of the MHC class I complex is endogenously produced and added in the host cell. Applicant argues that the claim amendments differentiate the claimed invention from the teachings of Celia because Celia does not teach the use of "endogenous" beta-2-microgobulin. Applicant's amendment and arguments fail to differentiate the claimed invention from the prior art. The claims are drawn to a complex comprising a liposome or artificial APC with an anchored MHC class I complex consisting of a heavy chain, beta-2-microglobulin and an associated antigenic peptide. The claims are not drawn to the method of making the product, but rather to the product itself. There is no physical difference between a beta-2-microglobulin produced endogenously in a host cell and a beta-2-microglobulin transfected into a host cell. Both can make a complex with an MHC class I heavy chain and an antigenic peptide. Similarly, Applicant's arguments that the Celia reference teaches only loading the antigenic peptide onto the MHC class I complex as opposed to in the host cell as in the instant specification does not differentiate the claimed complex from that of the prior art teaching because both methods result in a liposome with an attached MHC class I complex loaded with peptide. Accordingly, the resultant liposome or artificial APC would be the same irrespective of whether the beta-2-microglobulin is from an endogenous or exogenous origin or when the antigenic peptide became associated with the MHC class I. The claims are drafted in a "product-by-process" manner. However, the product remains the same regardless of the manner in which it was produced.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made

to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-9, 12-17, 31-36 and 39-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Celia et al. (Proc. Nat. Acad. Sci. (USA) [1999] 96:5634-5639; AT on form PTO-1449, of record) in view of Albani (WO 00/23053; D on form PTO-1449, of record).

It was previously stated: "Celia has been discussed supra. Celia does not teach additional signal molecules on the liposomes for manipulating intensity and quality of the T cell response.

Albani teaches complexes comprising a liposome and at least one MHC-peptide complex that is tagged with cholera toxin that anchors the MHC-peptide complex via interaction with GM-1 protein in the bilayer of the liposome (Figures 1-7B; page 12, lines 11-24 and page 21, lines 15-18 in particular) [claims 1, 2, 4-7, 12-17, 31]. Albani further teaches the inclusion of signal molecules in the liposome membrane to manipulate the intensity and quality of the T cell response (page 19, lines 26-27 in particular). Albani further teaches that the liposome-based complexes were capable of interacting with T cells (Figures 16A-18D in particular).

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to use the make a liposome complex comprising an MHC-peptide complex for modulating T cell activity because Celia teaches the making of liposomes comprising MHC:peptide complexes in the correct orientation on their surface and Albani teaches that liposomes with MHC:peptide complexes properly oriented on their surface can effectively interact with specific T cells. one would have been motivated to use the histidine tail construct of Celia versus the cholera toxin construct of Albani with a reasonable expectation of success by the fact that the Celia construct does not involve a toxin in its manufacture.

Claims 4-7 and 12-17 are drafted in a product-by-process manner, drawn to the liposome/MHC/ peptide complex, but drafted in a manner reciting the manner of producing the complex. Claims 4-7 and 12-17 are included in this ground of rejection because the product is perceived to be the same, irrespective of the manner in which it is made absent a showing that the method of manufacture necessarily results in a product materially different from the prior art product."

Applicant's traversal of Celia has been discussed supra. Applicant agrees that Albani teaches liposomes containing MHC:peptide complexes as well as accessory molecules and co-stimulatory molecules. Applicant argues that Albani fails to make up for the alleged deficiencies of Celia because Albani teaches only full-length MHC molecules and the loading of peptide onto the complexes after the complexes were put into liposomes. However, as explained supra, Celia is not deficient in regard to the claimed complexes with respect to the length of the MHC and to the loading of the peptide, and Albani was relied upon solely to show that the artisan would have found it obvious to combine accessory

molecules and co-stimulatory molecules with MHC:peptide complexes in an artificial APC or liposome vehicle for presentation of antigen to T cells. accordingly, the combination of references is maintained.

5. **The following NEW GROUNDS of rejection have been necessitated by Applicant's amendment.**

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-16 and 31-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Base claims 1 and 31 have been amended to recite and newly introduced base claims 32 and 42 have been drafted to recite "...a recombinant soluble **MHC heavy chain** molecule containing a tag for anchoring..." Applicant has introduced this language in an attempt to differentiate the claimed invention from the cited teachings of Walter et al (J. Immunol. Meth. [1998] 214(1-2):41-50; V on form PTO-892 of record), which attaches a comparable tag sequence to the beta-2-microglobulin member of the complex. However, review of the specification does not reveal support for specifically attaching the label to the "heavy chain" as opposed simply to the MHC complex. Accordingly, the recitation constitutes new matter and must be removed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-16 and 31-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Base claims 1, 31, 32 and 42 are ambiguous and unclear in the recitation of a liposome or artificial APC comprising an "endogenously produced peptide." The term "endogenously" is well understood in the art as referring to a product of internal genomic material. The liposomes and artificial APCs of the claimed invention are described as having been formed after the assembly of the MHC complexes and are, accordingly, devoid of genomic material. Accordingly, it would be impossible for the liposomes and artificial APCs to comprise any peptides that are endogenously produced. Applicant may clarify by, instead, reciting --a peptide produced endogenously in the host cell--.

Conclusion

8. No claim is allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
April 13, 2005

DAVID SAUNDERS
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